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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/501,171	02/09/00	GEORGE-HYSLOP	P 1034/1F811-U

EXAMINER	
TURNER, S	
ART UNIT	**PAPER NUMBER**
1647	10

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DATE MAILED: 10/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev. 2/95)
*U.S. GPO: 2000-473-000/44602

Office Action Summary	Application No. 09/501,171	Applicant(s) ST. George Hyslop
	Examiner Sharon L. Turner, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 7-12-01 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-13 is/are pending in the application.

4a) Of the above, claim(s) 6-13 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-5 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Sequence Requirements

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

In particular the sequence listing discloses SEQ ID NO's: 1-6. However, the specification only references/describes SEQ ID NO's: 3-6. The specification is required to describe and reference SEQ ID NO's: 1 and 2.

Election/Restriction

2. Applicant's election without traverse of Group I, claims 1-5 in Paper No. 9 is acknowledged.

3. Claims 6-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO: 4 which corresponds to a full length hNPRAP peptide. This SEQ ID NOs meet the written description provisions of 35 USC 112, first paragraph. However, the claims are directed to or encompass the generic recitation of hNPRAP peptides corresponding to sequences from other species, mutated sequences, allelic variants, splice variants, and sequences with various degrees of identity, similarity or homology. None of these generic sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:4 of the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic and amino acid sequences and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires

more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific nucleic and amino acids are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO:4, but not the full breadth of the claims as encompassed by hNPRAP meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

6. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The specification states at p. 4, lines 11-16 that "over-expression of hNPRAP, or functional derivatives thereof containing one or more armadillo repeats, causes the development of numerous long, dendritic processes which typically terminate upon distantly located cells," and that "the hNPRAP induced cellular extensions are highly similar to the axonal sprouting seen during neuronal regeneration and synapse formation." Yet, the specification fails to teach those cell types which exhibit this response upon contact with hNPRAP (i.e., fails to teach that neuronal cells respond) and fails to show any exemplary evidence of neuronal regeneration or synapse formation as claimed. As noted by Jackowski neuronal cells and especially CNS neuronal cells differ from other cell types as neurons are inhibited in regenerative capacity. Thus, the specification fails to evidence the claimed effects of stimulating growth of nerve cells absent evidence of such in neuronal cells.

Further, the examiner notes that the observed effects noted in the specification are generically displayed by a multitude of cells under various conditions, see in particular McDonald et al., Annals of the Rheumatic Diseases 1988 March, 47(3):232-40, Tanaka-Matakatsu et al., 1996 Dec., 122(12):3697-705, and Stamatoglou et al., Exp. Cell Res., 1992 Jan, 198(1):179-82, and that the noted effects in response to hNPRAP are not distinct among neuronal cells. Thus, the literature does not support a conclusion that the hNPRAP molecule is any more effective in promoting nerve cell growth, neuronal regeneration or synapse formation than for any of the other art noted effects including dendritic type outgrowth as indicated by filopodial extension in synoviocytes, drosophila trachea, or hepatocytes. Indeed it appears that the change

in morphology noted by applicants specification may be an inconsequential event in the normal growth, differentiation, spreading or chemotaxis of any cell which as noted occurs in response to modification in microtubules and actin cytoskeleton. Thus, the based on the specifications limited observations the skilled artisan would fail to find the specifications evidence indicative of neuronal cell growth, regeneration or synapse formation as claimed.

The specification states at p. 4, lines 23-27 that hNPRAP is known to interact with Presenilin I and II and that the domain of the PSI protein that interacts with hNPRAP has also been shown to interact with other proteins such as armadillo repeat proteins, p0071 and β-catenin, hNPRAP presumably being of such a family and merely requiring the armadillo repeats for the stimulation of neuronal regeneration and axon sprouting, specification p. 5, lines 16-28.

However, as taught by Paffenholz et al., (IDS) the plakoglobin/armidillo multigene family is made of a growing number of very different proteins which are divergent in function and independent in structure from each other, see in particular Introduction, p. 293-294. Paffenholz et al., clearly recognize armadillo repeat proteins, but fail to recognize neuronal growth as a function of such proteins. With this in mind, it is noted that applicants claims encompass peptides of undefined variable structure as encompassed by the generic recitation of hNPRAP. Yet, the skilled artisan readily recognizes the unpredictable nature of protein chemistry. As noted by Skolnick et al., Trends in Biotech., 18(1):34-39, 200 even in highly related protein families, structural modifications by even a single amino acid substitution may lead to functional changes in biological activity, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39,

2000. Thus, the specification fails to teach the purported activities for the divergent molecules as encompassed by the claims.

Thus, without further undue experimentation the skilled artisan could not make and use the claimed invention without undue experimentation.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite hNPRAP. However, the specification fails to teach the structural meets and bounds of the generic recitation. Thus, the skilled artisan cannot readily discern the scop of the molecules intended to be encompassed by the claims. Clarification is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) as being anticipated by J. Regino Perez-Polo, US 5,475,088, Dec. 12, 1995.

J. Regino Perez-Polo teach multiple peptides which effect nerve cells by stimulating dendritic growth, cell survival, the promotion of axonal regeneration and synapse formation including peptides derived from nerve growth factor receptor, nerve growth factor and brain derived neurotrophic factor, see in particular Abstract, Background, columns 1-7 and Summary, column 8. The molecules cannot be excluded from applicants generic recitation of hNPARP which lacks any notable structure and thus, the reference teachings anticipate the claimed invention.

Status of Claims

11. No claims are allowed.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
September 25, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud